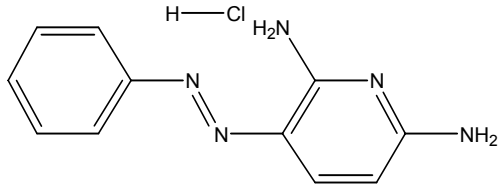
PHENAZOPYRIDINE HYDROCHLORIDE
CAS No. 136-40-3
First Listed in the *Second Annual Report on Carcinogens*



CARCINOGENICITY

Phenazopyridine hydrochloride is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.24, 1980; IARC S.4, 1982; NCI 99, 1978; IARC S.7, 1987). When administered in the diet, phenazopyridine hydrochloride increased the incidences of hepatocellular adenomas and carcinomas in female mice and adenomas and adenocarcinomas of the colon and rectum in rats of both sexes.

There is inadequate evidence for the carcinogenicity of phenazopyridine hydrochloride in humans. (IARC S.7, 1987). In one limited epidemiological study, no significant excess of any cancer was observed among 2,214 patients who received phenazopyridine hydrochloride and were followed for a minimum of 3 years.

PROPERTIES

Phenazopyridine hydrochloride occurs as brick-red microcrystals or powder with a violet luster and a slightly bitter taste. It is slightly soluble in cold water and ethanol, soluble in boiling water, acetic acid, glycerol, ethylene glycol, and propylene glycol, and insoluble in acetone, benzene, chloroform, diethyl ether, and toluene. The commercial compound may contain some ß,ß′-bis(phenylazo)-α,α′-diaminopyridine; the free base is not available commercially. Phenazopyridine hydrochloride decomposes at 235^{o} C and emits toxic fumes of nitrogen oxides (NO_x) and hydrochloric acid. It is sensitive to air and light.

USE

Phenazopyridine hydrochloride has been used for 40 years as an analgesic and antiseptic drug, either alone or in combination with sulfonamides and antibiotics, to reduce pain associated with urinary tract infections. It is useful because of its bacteriostatic action in both acid and alkaline urine. Its local effect may be an anesthetic action (IARC V.24, 1980; Kirk-Othmer V.7, 1979).

PRODUCTION

The USITC does not currently list any producers or production volumes for phenazopyridine hydrochloride. However, Chem Sources USA directory identified three companies as producers and one as a supplier in 1986 and 1984 (Chem Sources, 1986; Chem

Sources, 1984). In 1983, U.S. imports of phenazopyridine hydrochloride totalled over 17,000 lb (USITCa, 1984). In 1980, domestic production was estimated to be 22,000 to 110,000 lb/yr (IARC V.24, 1980). Data from the National Prescription Audit indicated that retail pharmacies dispensed 4.4 million prescriptions for the compound in 1980, with an average adult dose rate of 200 mg three times daily. The National Disease and Therapeutic Index reported in 1980 that hospital usage accounted for 21% of the chemicals use. In 1979, two companies reported production of an undisclosed amount of phenazopyridine hydrochloride. In 1978, imports of the compound through principal U.S. customs districts were reported by the USITC to total 15,400 lb (IARC V.24, 1980). Phenazopyridine hydrochloride was not included in the 1979 TSCA Inventory.

EXPOSURE

The primary routes of potential human exposure to phenazopyridine hydrochloride are ingestion, dermal contact, and inhalation. The usual adult oral dosage is 200 mg three times/day; the dosage for children is 12 mg/kg divided into three daily doses. Phenazopyridine hydrochloride is also used as a urinary antiseptic in a dose of 300 mg/day (IARC V.24, 1980). Potential occupational exposure may occur during production, formulation, packaging, or administration of phenazopyridine hydrochloride. The National Occupational Exposure Survey (1981-1983) indicated that 2,547 workers, including 1,328 women, potentially were exposed to phenazopyridine hydrochloride (NIOSH, 1984).

REGULATIONS

EPA has proposed that phenazopyridine hydrochloride be subject to handling and report/recordkeeping requirements under the Resource Conservation and Recovery Act (RCRA). FDA has approved the use of phenazopyridine hydrochloride as a prescription drug for human use for symptomatic relief of pain and other discomforts arising from irritation of the lower urinary tract. FDA is considering labeling requirements for this drug concerning possible carcinogenicity and dose duration limitations. OSHA regulates phenazopyridine hydrochloride under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-118.